Trinity Delta

Scancell

Opening new pathways in immuno-oncology

Scancell has two promising technology platforms for therapeutic vaccines that have the potential to treat many cancers, either as monotherapy or in combination with checkpoint inhibitors. Many therapeutic vaccines have failed to fulfil their potential; but the strength of the cellular immune responses stimulated by both ImmunoBody and Moditope, and the resultant anti-tumour activity observed to date in clinical and preclinical studies augers well. The financial issues that have hindered development of these products are being overcome, so a Phase II study with ImmunoBody SCIB1 and a Phase I/II with the first Moditope product are expected to start during CY19. We value the company, using a risk-adjusted DCF model, at £82.0m, or 21.1p a share.

Year-end: April 30	2017	2018	2019E	2020E
Sales (£m)	0.0	0.0	0.0	0.0
Adj. PBT (£m)	(4.5)	(4.9)	(8.6)	(7.6)
Net Income (£m)	(3.5)	(4.2)	(7.1)	(6.4)
Adj. EPS (p)	(1.4)	(1.3)	(1.8)	(1.6)
Cash (£m)	2.7	10.3	4.3	10.0*
EBITDA (£m)	(4.5)	(4.9)	(8.6)	(7.6)

Source: Trinity Delta; Adjusted numbers exclude exceptionals; * Cash in FY20 includes a capital increase of £12m

- **Therapeutic vaccines could expand immuno-oncology market** Immuno-oncology (IO) therapies, in particular checkpoint inhibitors (CI) such as Keytruda, have transformed the treatment of many cancers in recent years, converting the disease into a chronic condition. However, only 40% of patients, at best, in a given cancer indication currently benefit from immuno-oncology therapies. Therapeutic vaccines have the potential to significantly improve the proportion who benefit, by initiating immune responses against a tumour and converting "cold" cancers into "hot" ones.

- **ImmunoBody and Moditope products have clear potential to deliver** Historically some patients have responded well to therapeutic vaccines, but too few have benefited for the vaccines to be commercial successes. Preclinical data with the ImmunoBody and Moditope platforms show that both generate very potent cellular immune responses against tumours. The first ImmunoBody, SCIB1, has also produced promising clinical results in a Phase I/II study, which compares well to those observed with checkpoint inhibitors, while being much better tolerated.

- **Clinical trials due to begin shortly** Two trials with ImmunoBody are planned; the first with SCIB1 in combination with Keytruda in melanoma patients is anticipated to start in H119, and the second with SCIB2 in NSCLC will be conducted by CRUK. The first Moditope product is also expected to enter the clinic in CY19, in patients with solid tumours, such as triple negative breast cancer and ovarian cancer. Data readouts from the trials are expected from H120 onwards. The company also has a potentially lucrative collaboration with BioNTech, the major European IO company.

- **rNPV model suggests a valuation of 21.1p/share** We value Scancell based on a rNPV and sum-of-the-parts methodology, with conservative assumptions. Based on our model we value Scancell today at £82.0m, equivalent to 21.1p a share. The initiation of clinical trials and data should act as share price catalysts.

Price	8.10p
Market Cap	£31.4m
Enterprise Value	£23.5m
Shares in issue	387.8m
12 month range	7.60-19.47p
Free float	95%
Primary exchange	AIM London
Other exchanges	N/A
Sector	Healthcare
Company Code	SCLP.L
Corporate client	Yes
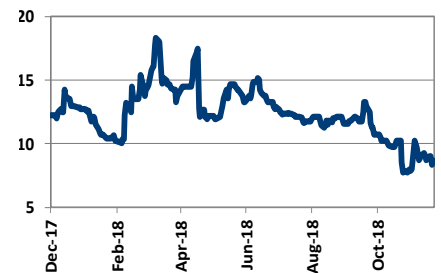
Company description

Scancell is a clinical-stage immuno-oncology specialist that is developing two innovative and flexible therapeutic vaccine platforms. ImmunoBody and Moditope induce high avidity cytotoxic CD8 and CD4 responses, respectively, with the potential to treat various cancers.

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Investment case

Scancell is a clinical-stage immuno-oncology specialist. It was founded in 1997 as a spin-out of research led by Prof Lindy Durrant at the University of Nottingham. In 2006 the pipeline of direct-killing antibodies was sold to Arana Therapeutics and research efforts focused on the ImmunoBody and Moditope cancer vaccine programmes. The two platforms are very different - ImmunoBody employs CD8 T-cell pathways whilst Moditope effects are mediated via CD4 pathways - with clear differentiation and benefits over previous therapeutic vaccine approaches. Both platforms should have broad applicability in many forms of solid tumours.

Scancell initially listed on PLUS in 2008 and moved to AIM in 2010. Over £37m has been raised in equity since inception with £8.7m raised in the past year. The development programme planned for the near-term suggests a funding requirement of £12m. The leading shareholders are Calculus Capital (12.9%), City Financial (5.6%), Legal and General (4.7%) and Hygea VCT (3.4%). The company is based in Oxford and Nottingham, and has 21 full-time employees.

Valuation

We value Scancell using an rNPV of the four lead indications from the two vaccine platforms, which are then netted out against the cost of running the business and net cash. The success probabilities in each known indication are based on standard industry criteria for each stage of the clinical development process, but flexed to reflect their differing characteristics. We have employed conservative assumptions throughout; for example, erring on the cautious side for factors such as the timing of clinical studies, market launches, adoption curves, and patient penetration. Despite such a deliberately cautious approach we currently value Scancell at £82.0m, equivalent to 21.1p per share.

Financials

Following a share placing of £6.9m (net) in April, Scancell had cash of £10.3m at FY18 year-end. A further £1.1m (net) was raised in May. The forecast cash burn of around £6.4m per annum over the next 24-36 months suggests a runway through to early 2020. However, in addition to the funds employed in progressing the clinical programmes to the next value-inflection points, we would argue that the opportunities that are presenting themselves to develop the two platforms would warrant a strengthening of the capital base. Our forecasts suggest a funding requirement of c £12m within the next 12 to 24 months.

Sensitivities

Scancell's therapeutic vaccine programmes are at the cutting edge of immuno-oncology and, inevitably, carry a higher risk profile. This area of science is increasingly crowded and competitive, with multiple players (ranging from large pharmaceutical groups to biotech companies and even well-funded academic centres) vying to develop the definitive break-through. Equally, the usual industry risks associated with clinical trial results, navigating regulatory hurdles, ensuring sufficient financing is in place, partnering discussions and, eventually, the exit strategy, still apply. Our main sensitivities are detailed later (in the body of the note), with particular emphasis on each individual programme.

Scancell: innovative immunology

The potential of immune activation to treat cancer is now fully appreciated, because of the impact of checkpoint inhibitors. However, a disappointing number of patients currently fail to benefit from their use; Scancell's ImmunoBody and Moditope platforms could provide part of the solution. The company has learnt from past failures of other therapeutic vaccines. Both platforms have delivered promising preclinical data and, and in the case of ImmunoBody SCIB1, clinical data. Financial issues are gradually being overcome by the new management, so that Scancell now aims to initiate two new clinical trials in 2019: a Phase II study with an ImmunoBody in combination with the checkpoint inhibitor pembrolizumab, and the first clinical trial with a Moditope. We value Scancell, using a rNPV approach, at £82.0m, or 21.1p/share

Immunotherapies are changing our perceptions of cancer but…

The treatment of many cancers is being revolutionised by immunotherapies, such as the checkpoint inhibitors pembrolizumab (Merck's Keytruda) and nivolumab (BMS's Opdivo). These therapies can improve the long-term survival of cancer patients, but disappointingly only c 40% of patients achieve such an outcome in melanoma (the most immunogenic tumour), and there is no benefit at all in some cancers. The challenge for immuno-oncology is now to improve the proportion of patients that respond well to therapy.

…there are still challenges to overcome

There are numerous methods being assessed currently to make tumours more immunogenic. One approach is to directly prime an anti-tumour response using therapeutic vaccines. This class of treatment had fallen out of favour, after late stage clinical trials failed to confirm the promise in Phase I/II studies. But, major collaborations in the field involving Merck & Co and Roche show there is renewed interest, as the immune system is better understood.

Learning from others' setbacks

A key issue of earlier therapeutic vaccines was that, for various reasons, they did not generate a predictable, strong immune response. Scancell has learnt from the setbacks, and created two novel classes of vaccine, ImmunoBody and Moditope.

ImmunoBody generate a strong and predictable immune response

ImmunoBody vaccines have an elegant design to ensure the efficient cross-presentation of specific epitopes (peptide sequences from proteins), and a consistently strong anti-tumour immune response. Promising activity was seen in a monotherapy Phase I/II study in melanoma, but the real potential of ImmunoBody is in combination with checkpoint inhibitors. This will be explored in two trials with different ImmunoBodies, SCIB1 and SCIB2.

Moditope have generated impressive preclinical data

Moditope is a totally different class of therapeutic vaccine, and potentially more promising. It effectively generates an immune response against cells undergoing autophagy (a vital process for most cancer cells) by targeting a modification on proteins. Exceptional results have been observed in preclinical studies and the first Moditope is expected to enter the clinic in CY19

A deceptively simple approach that will be validated by trial data

The company has raised £37m to date but we believe it has been under-funded historically, which has, in our view, caused delays to the development of the programmes. We estimate it needs an additional £12m over the next 24-36 months. The new management is addressing this issue and the company is regaining momentum as shown by the clinical trials due to start in 2019.

Harnessing the immune system for solid tumours

An admirably simple strategy that will be validated by clinical trials

Scancell is developing therapeutic vaccines to treat solid tumours, using its two proprietary technology platforms, ImmunoBody and Moditope. The lead ImmunoBody programme has delivered promising Phase II results in metastatic melanoma, and trials with the first Moditope are due to start during CY19. Based on the data to date, products from both platforms have potential as monotherapies; but, we believe, their greatest prospects are probably in combination with checkpoint inhibitors and/or other treatments such as adoptive T-cell therapies.

Prophylactic cancer vaccines are well established immune therapies

Vaccination is clearly well-established for the prevention of diseases. It has proven to be particularly effective as prophylactic treatments against various viruses in reducing and even eradicating diseases. Prophylactic vaccines against HPV (Merck's Gardasil and GSK's Cervarix) have also been used to prevent women developing cervical cancer, which is caused by the HPV virus. However, progress with the development of therapeutic vaccines, to stimulate a person's immune system to attack their cancer, has to date proved disappointing.

Harnessing the immune system is not a new idea...

The interest in therapeutic vaccines to treat cancer can be traced back to 1891, when Dr William Coley inoculated cancer patients with Coley's Toxins and achieved some remarkable recoveries. Since then, many companies have attempted to develop such treatments, and too often promising results in early clinical trials were followed by disappointment in Phase III. In fact, many people doubted the immune system could be harnessed to treat cancer, until Provenge (sipuleucel-T), the autologous dendritic cell vaccine, was approved for the treatment of metastatic castration resistant prostate cancer in 2010.

...but has only really come of age in the last decade...

In the same year, BMS published the results of a Phase III study in malignant melanoma with the CTLA-4 antibody ipilimumab (Yervoy), which led to the transformation of the field of oncology. The main focus of drug development in oncology was to extend median overall survival as attempts to prolong long-term survival had largely failed; however, the data from this study showed that it was possible to significantly improve long-term survival by enhancing the activity of a person's immune system.

...with several well-established blockbuster products

Since then, checkpoint inhibitors have become a cornerstone of many oncology therapies, in particular the PD-1 inhibitors, pembrolizumab (Merck's Keytruda) and nivolumab (BMS's Opdivo). There has also been the launch of the first CAR-T therapies (Novartis' Kymriah and Gilead's Yescarta), for the treatment of a few haematological cancers. All of these treatments have the potential to convert cancer into a chronic disease, with which people can live.

**Challenges and frustrations are still very evident**

Despite the tremendous progress in immuno-oncology in the last eight years, there is still a frustration that more cancer patients do not benefit from the checkpoint inhibitors. With checkpoint inhibitors, it has generally been difficult to increase the proportion of patients who benefit from such treatment to above c30%; and in the case the current CAR-T therapies, they are too expensive (as well as needing many technological issues still to be overcome) for them to become a mainstream treatment for most cancers.

In melanoma, which is the most immunogenic tumour, it has been possible to increase long-term survival to c60% by combining PD-1 and CTLA-4 antibodies

(nivolumab/pembrolizumab and ipilimumab). However, this is also associated with a very high level of serious adverse events (Grade 3/4); in the CHECKMATE-067 Phase III trial, 72% of patients receiving nivolumab and ipilimumab experienced such events compared to 44% in the nivolumab monotherapy arm. This highlights the issues faced in immuno-oncology.

The goal is a powerful immune response yet with tolerability

Both nivolumab and ipilimumab relieve the immunosuppression that affects a person's T-cell response, which is part of the adaptive immune response (Exhibit 1). It is the adaptive immune system that provides a specific, targeted response to infections and that has an immunological memory to respond rapidly to previously encountered antigens. T-cells are designed to provide a potent, cellular response against infected cells, but there are also many severe autoimmune diseases caused by inappropriate immune activation, such as rheumatoid arthritis and multiple sclerosis. So, the challenge in the field of immuno-oncology is to direct a potent immune response against a tumour, while having a manageable tolerability profile.

Exhibit 1: The innate and adaptive immune systems
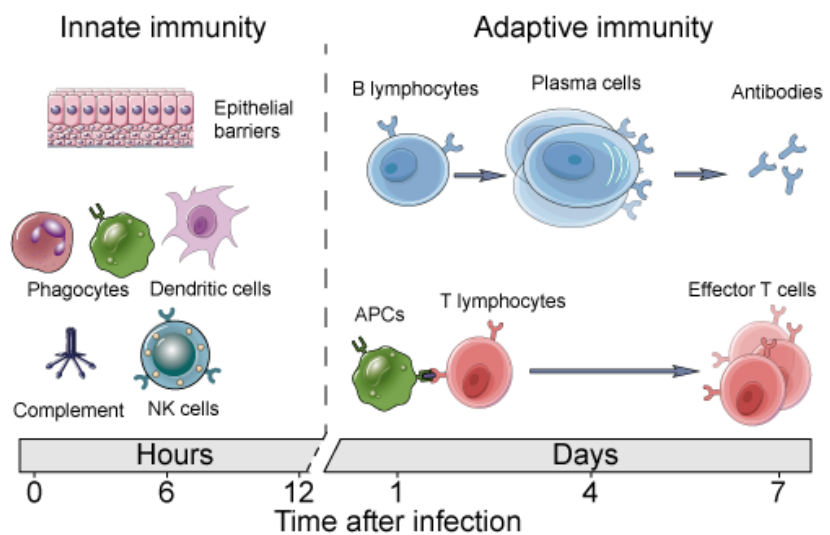
Source: Creative Diagnostics

Greater understanding of the immune system has been the key

This, in turn, has led to greater interest in therapeutic vaccines and ways of stimulating the immune system to target the tumour, which could work synergistically with checkpoint inhibitors. Fortunately, the better understanding of the immune system has resulted in new approaches, so the next generation of therapeutic vaccines should deliver more consistent, positive results than before.

The major challenge in developing therapeutic vaccines for oncology is to increase the activity of the immune response against tumour cells, which by definition originated from a person's own normal tissues. The immune system has evolved careful mechanisms to prevent it targeting healthy host tissues, which need to be circumvented. Exhibits 2 and 3 overleaf detail the main classes of T-cells and a summary of the T-cell response.

A sustained effective response depends on the antigens selected

To achieve an effective and sustained anti-tumour immune response, it is generally required that high-avidity, cytotoxic T-cells are stimulated. This requires the careful selection of cancer antigens or epitopes (short amino acid sequences that make up part of the protein) to stimulate an immune response against a tumour that presents the same epitopes. On top of this, the delivery mechanism needs to be considered carefully.

Exhibit 2: Main classes of T-cells

Product	Notes
Helper T-cells (Th)	Th cells act as co-ordinators of immune responses, secreting cytokines, which can lead, for example, to a pro-inflammatory Th1 response (including activating cytotoxic T-cells) or anti-inflammatory Th2 response (eosinophilic response).
Regulatory T cells (Treg)	Treg cells are negative regulators of an immune response, counteracting the activity of Th cells.
Cytotoxic CD4 T cells (CD4 Tc, CTL)	CD4 CTL bind to the target cell by the TCR (T-cell receptor) binding to the MHC II/antigen complex, causing cytotoxins such as perforin and granzymes to be secreted, which induce apoptosis (programmed cell death) of the target cell.
Cytotoxic CD8 T cells (CD8 Tc, CTL)	CD8 CTL are similar to CD4 CTL, except that they normally bind to MHC I/antigen complexes. CD8 CTL are the prinicipal mediators of cellular immune responses.

Source: Trinity Delta

Exhibit 3: Summary of T-cell immune response

- **Antigen processing** – Antigen presenting cells (APCs), such as dendritic cells and macrophages, internalise proteins by endocytosis or phagocytosis.

- **Antigen presentation** – The internalised proteins are broken down into short peptides, which bind to the MHC I and MHC II proteins. The MHC-I and MHC-II complexes are transported to the cell's membrane to interact with T-cells.

- **Selection of T-cells in cortex of thymus** – If a TCR (T cell receptor) on an immature T-cell binds to the MHC I/II complexes, that cell survives and advances into the medulla of the thymus, otherwise the T-cell will die through apoptosis. – **Positive selection.**

- **Deletion of T-cells in medulla of thymus** – The immature T-cells with a high avidity for self-antigens die through apoptosis – **Negative selection** – the remainder are released into the body.

- **Activation of cytotoxic T-cells –** In response to the Th-cell detecting the specific MHC/epitope complex to which its TCR binds, the Th-cell releases cytokines that activate cytotoxic T-cells (this process is counteracted by Tregs).

- **Cytotoxic activity of T-cells –** If an activated cytotoxic T-cell (Tc) finds a cell that is presenting the specific MHC/epitope complex it secretes cytotoxins, such as perforin and granzymes, thereby inducing apoptosis (programmed cell death) of the target cell.

Source: Trinity Delta

High avidity is necessary for effective therapeutic vaccines

Much has been learnt from the disappointing results with earlier attempts to develop therapeutic vaccines (Exhibit 4). For example, the discussion around the best epitopes has moved from tumour-associated antigens (TAA) to neo-antigens. The issue with using TAA is that most are recognised as self-antigens that are often expressed, albeit at low levels, in various other tissues, so that it is unlikely that there will be high avidity response against the TAA. In contrast, neo-antigens are by definition new ones found on tumour cells, which are not normally found in any tissues, so vaccination with a neo-antigen should result in a high avidity response.

Exhibit 4: Potential reasons for a lack of efficacy with therapeutic vaccines

Reason for limited efficacy	Explanation
Epitope recognised as self	Self-antigens normally result in an immune response with a moderate avidity and limited activity, due to negative selection of high avidity T-cells in the thymus.
Use of whole proteins	The use of whole proteins can give rise to a broader T-cell response, compared to the use of peptides; however, most of the epitopes from the whole protein will be self-antigens, which will not result in a high avidity response. Alternatively, immunodominance can occur, resulting in a T-cell response against a small number of epitopes, which might not be the correct ones for anti-tumour efficacy.
Repertoire	Despite the diversity and breadth of epitopes that different TCRs can recognise, it is finite and there are some epitopes to which TCRs tend not to bind.
Delivery system – viral system	Viral delivery systems, such as MVA, can act as potent adjuvants, however the patient might develop a response against the virus rather than the protein/epitope of interest.
Delivery system – depot delivery	A depot delivery system can induce a strong immune reaction, however the depot can act as a sink for the induced T-cell response.
Single-antigen vaccination	Not all tumours express the same antigens, and there is intra-tumour heterogeneity, so few patients might respond if a single antigen is targetted rather than multiple antigens. Similarly, clonal escape (formation of clones of tumour cells that do not express a specific antigen) is likely to be more common with a single- than with multiple-antigen vaccinations.

Source: Trinity Delta

ImmunoBody generates a high-avidity CD8 T-cell response

The first of Scancell's technology platforms, ImmunoBody, is designed to induce a high avidity cytotoxic CD8 T-cell response against epitopes with very restricted expression patterns. The epitopes are not actually neo-antigens, but it had been observed that some patients that had spontaneous tumour regression had developed immune responses against the selected epitopes. The features of ImmunoBody are discussed below; but Exhibit 5 provides an indication of the strength of the immune response that can be stimulated with the leading ImmunoBody, SCIB1.

Exhibit 5: Comparing the strength of T-cell response of ImmunoBody SCIB1 with three other forms of vaccination in preclinical studies
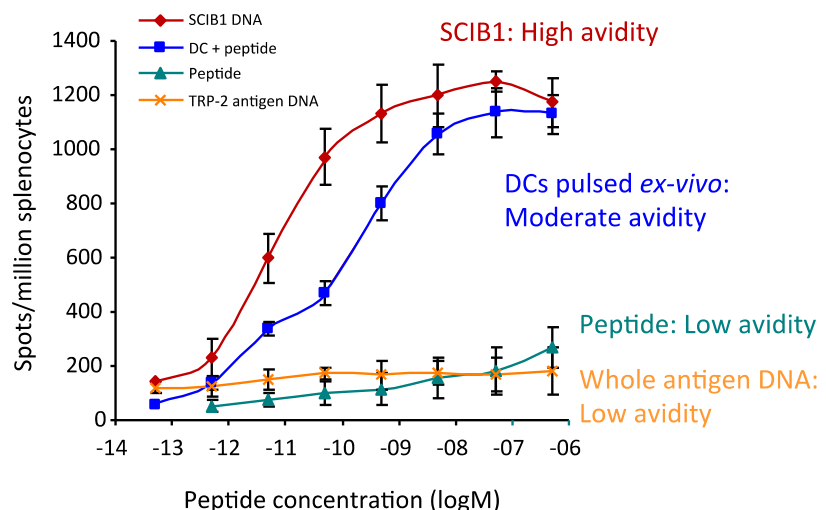
Source: Scancell; Notes: DC – Dendritic cell vaccine

Moditope stimulates a targeted CD4 T-cell cytotoxic response

The second platform, Moditope, was identified with an element of serendipity while trying to improve the ImmunoBody technology. Moditope products stimulate a cytotoxic CD4 T-cell response and not a cytotoxic CD8 T-cell

response, unlike ImmunoBody and other therapeutic vaccines that have been developed. As such, Moditope is a totally different class of therapeutic vaccine, and the preclinical data so far suggests these vaccines could be even more potent than equivalent ImmunoBody vaccines.

Investors and "big pharma" hold divergent views on therapeutic vaccines

It should be noted that, whilst many investors are particularly cautious about the potential of therapeutic vaccines to treat cancer, this is not a sentiment shared by "big pharma" companies focussed on immunotherapy. This is demonstrated by the major collaboration between Merck & Co and Moderna (initiated in June 2016 and extended in May 2018), and Genentech and BioNtech (formed in September 2016) in the field of mRNA cancer vaccines.

Pipeline and technology platforms

Management changes have brought focus and dynamism

Scancell's pipeline is regaining momentum following recent management changes and subsequent capital raises, with two new trials expected to be initiated by the company in the next year, as detailed in Exhibit 6. They are assessing the potential of ImmunoBody SCIB1 in combination with a checkpoint inhibitor, and a first-in-man study with Moditope Modi-1, to assess safety and efficacy in up to three cancer indications.

Exhibit 6: Scancell's pipeline
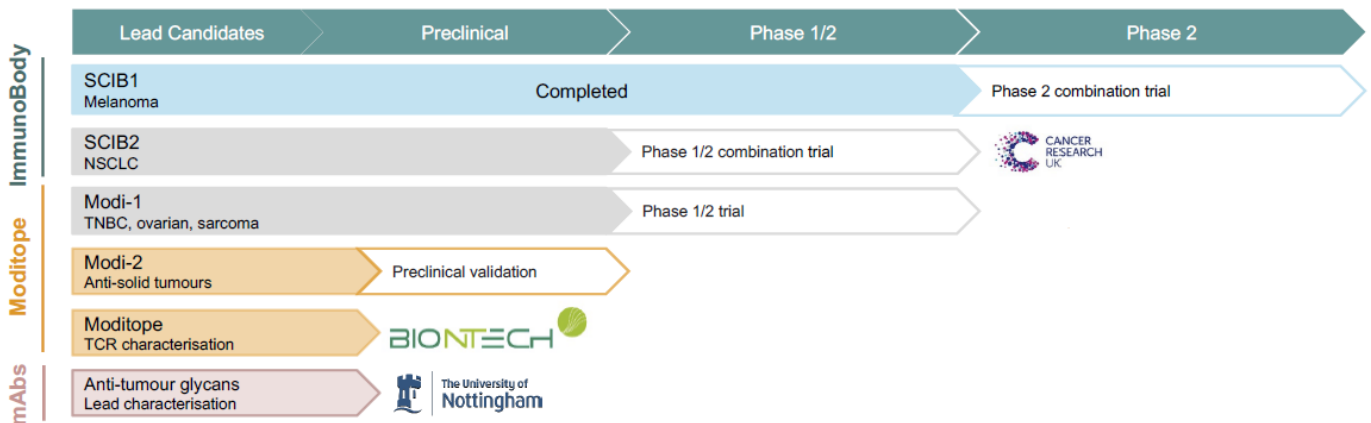
Source: Scancell

ImmunoBody platform and programme

An elegant and highly promising approach

ImmunoBody vaccines have an elegant design to generate high avidity T-cell responses capable of a broad anti-tumour effect. They are DNA vaccines that encode a protein in the form of an antibody, but the parts of the antibody that would normally bind to the target protein are replaced with epitopes from a cancer antigen (Exhibit 7).

Exhibit 7: The structure of the ImmunoBody
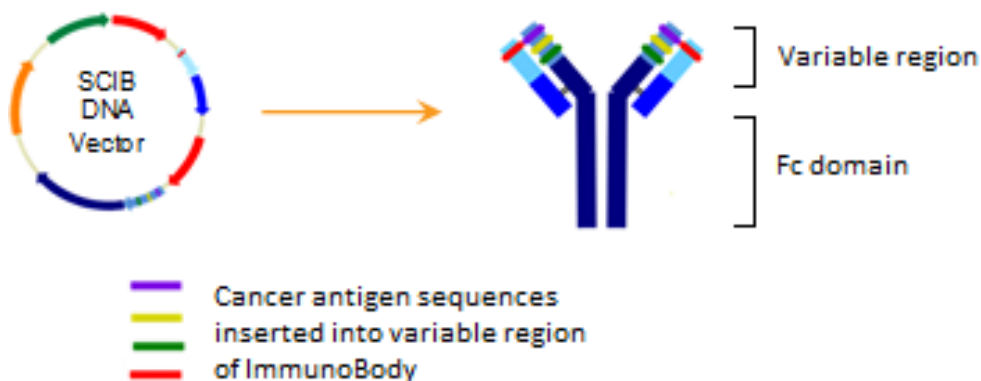
Source: Scancell; Trinity Delta

The key design features include:

- Epitopes that bind to both MHC I (for the CD8 T-cell response), and MHC II (for the CD4 Th-cell response);
- A DNA vaccine with motifs (eg GC rich regions) to ensure it is immunogenic, and taken up directly dendritic cells;
- Fc region of the protein form of an ImmunoBody targets activated dendritic cells.

High avidity results from cross presentation via multiple pathways

The most important aspect of the ImmunoBody is its ability to initiate both direct and cross-presentation of epitopes to T-cells. There are various pathways by which dendritic cells can process antigens, and the highest avidity T-cell response are generated if more than one pathway is used to present the same epitope. In the case of the ImmunoBody, the DNA form is taken up directly by dendritic cells and processed, and the protein form (which is produced at the site of the injection from the DNA) binds to the Fc receptors on dendritic cells leading to the cross presentation. (Exhibit 8). As a result of both the direct and cross-presentation, the T-cells not only have a higher avidity, but there are many more T-cells generated against the epitopes of interest.

Exhibit 8: The cross-presentation of epitopes by ImmunoBody
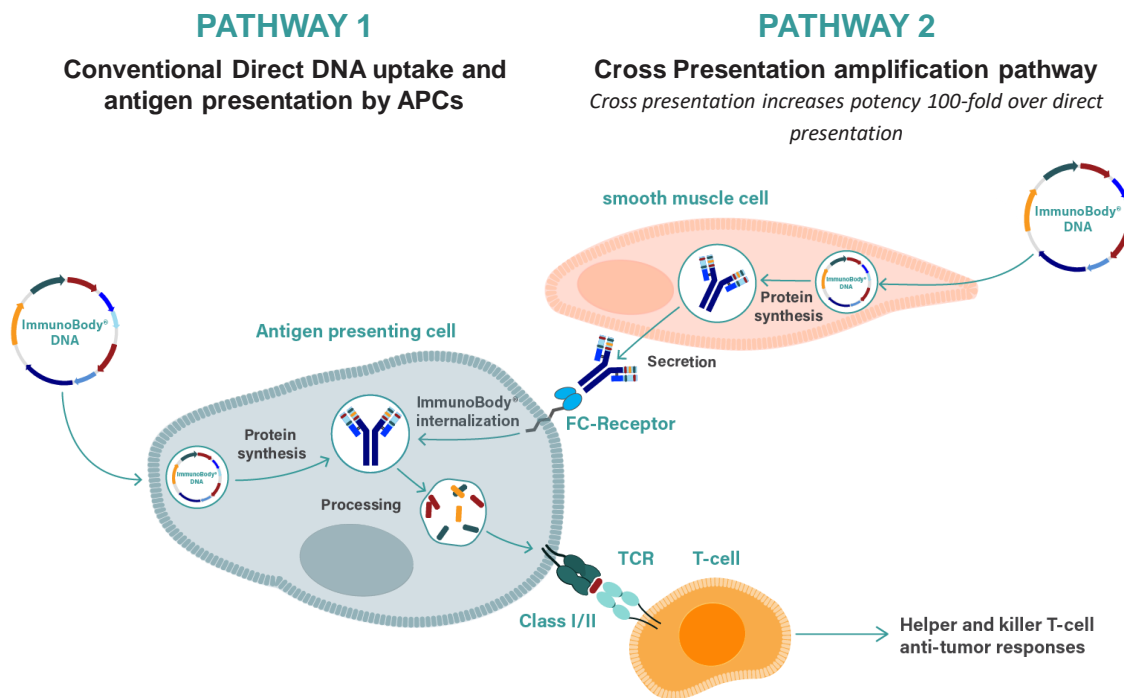
Source: Scancell

A potent and targeted cytotoxic response is generated

ImmunoBody generates both a cytotoxic CD8 cell response and a Th CD4 response. This is because the ImmunoBody vaccines have been created so that epitopes for both MHC I and MHC II complexes are produced once they have been broken down by the proteasomes. Epitopes for MHC I are normally 8-11 amino acids in length and generate a CD8 response, and epitopes for MHC II are usually 13-17 amino acids long and result in a CD4 response. The generation of both a Th and Tc cell response is important, as the Tc cells only become activated and able to destroy the tumour cells once Th cells recognise the appropriate epitope and secrete cytokines.

There are so far two ImmunoBodies in development:

- SCIB1, a vaccine incorporating specific epitopes from the proteins, gp100 and TRP-2, which were identified from the cloning of T-cells from patients who achieved spontaneous recovery from melanomas. Both proteins play key roles in the production of melanin in the skin.

- SCIB2, a vaccine incorporating epitopes from the cancer testes antigen, NY-ES0-1, which is normally only expressed in germline cells, and TCR proteins have been identified that bind to various NY-ESO-1 epitopes.

Results of Phase I trial comparable to those seen with checkpoint inhibitors…

The lead ImmunoBody, SCIB1, has completed a dose-escalation Phase I/II study in 35 patients with metastatic melanoma. Fifteen of the patients had tumours present and 20 had fully-resected disease and received doses ranging from 0.4mg/dose to 8.0 mg/dose. In the study, there was a dose dependent immune response to SCIB1 and an associated anti-tumour effect. Out of the 15 patients who had tumours present, one achieved a partial response and has survived for over five years, and five achieved stable disease, with two alive two years after therapy. Out of the 20 patients with fully resected disease, 15 were disease free after a median observation time of 37 months, and all were still alive (Exhibit 9).

Exhibit 9: Kaplan-Meier curves for (A) overall survival in all patients who had tumours and had received at least three doses (n=10); and (B) recurrence-free survival in patients fully resected tumours at study entry (n=20)

A.

B.
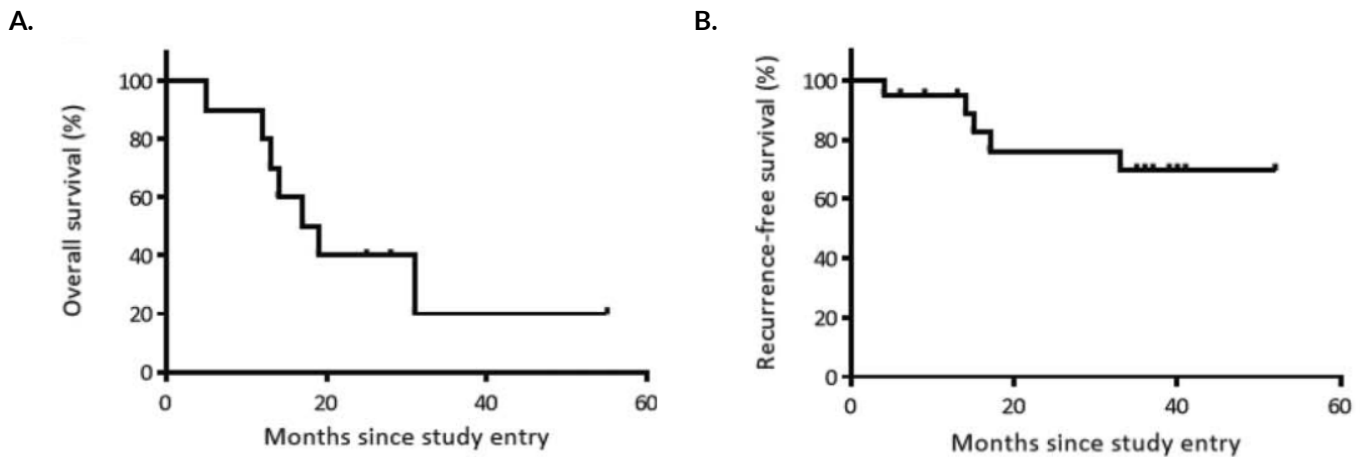
Source: Patel et al, Oncoimmunology 2018

It is difficult to compare the data from this study with those from other trials in the field. Having said that, the results appear comparable to those achieved with checkpoint inhibitors, such as ipilimumab (BMS's Yervoy), nivolumab (BMS's Opdivo) and pembrolizumab (Merck's Keytruda), and SCIB1 is much better tolerated.

…but without the side-effects, although some disliked the delivery device

There were no serious adverse events associated with SCIB1 therapy. The main adverse event was at the injection site, and was associated with the electroporation delivery system, Ichor Medical Systems' TriGrid. This delivery technology is able to improve the efficiency of the delivery of DNA vaccines by up to 1000-fold compared to standard needle delivery. However, it is associated with a minor electric shock in the arm, which caused 27 (77%) patients to suffer from an injection site haematoma, including 1 (3%) with a Grade III reaction. Also, one patient was only able to tolerate three immunisations with SCIB1, although five patients have had 15-17 immunisations.

**Unfortunate timing meant attention was drawn elsewhere**

Despite the promising signal from this Phase I/II trial, which was started in June 2010, development stalled due to manufacturing issues as a result of the extended duration of the study, and tremendous changes in the whole competitive landscape. Unfortunately for Scancell, it initiated the trial just before the results of the ground-breaking ipilimumab results were published, which caused the pharmaceutical industry to almost totally focus on checkpoint inhibitors in the field of immuno-oncology for several years. However, it is now becoming apparent that checkpoint inhibitors need complementary therapies to increase the proportion of patients that could benefit from immuno-oncology, and

additional funding means that a Phase II trial in metastatic melanoma in combination with checkpoint inhibitor pembrolizumab should start in H119.

Strong case for use in combination with checkpoint inhibitors

There is a clear rationale for using an ImmunoBody to prime an immune response against a tumour to enhance the efficacy of checkpoint inhibitors. This potential has been confirmed in preclinical studies; they suggest that SCIB1 and an anti-PD-1 antibody have similar activity as monotherapies (consistent with the Phase I/II data), and have a strong synergistic effect (Exhibit 10).

Exhibit 10: The activity of SCIB1 and anti-PD-1 checkpoint inhibitor in combination in preclinical studies
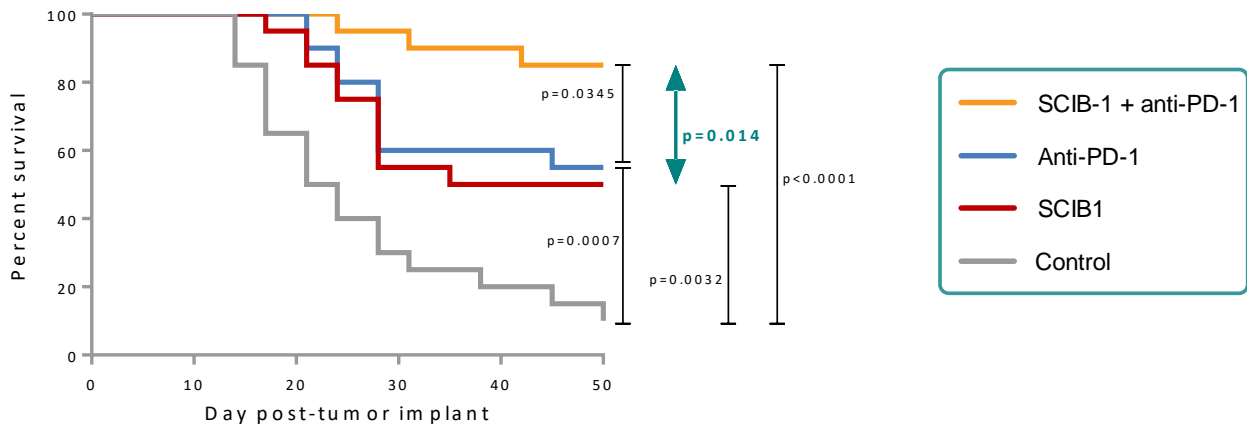
Source: Scancell

The new Phase I/II trial with SCIB1 will be in patients with unresectable stage III/IV melanoma, without any prior systemic treatment and suitable for treatment with pembrolizumab. During stage one of the study, six patients will be treated with a primary focus on safety. If the combination therapy has an acceptable tolerability profile, a further 19 patients will be treated. The dosing regimen is shown in Exhibit 11, and the trial will be considered a success if ≥12 patients respond to therapy, i.e. the anti-tumour activity of SCIB1 and pembrolizumab (anti-PD-1) is similar to that seen with the combination therapy of ipilimumab (anti-CTLA-4) and nivolumab (anti-PD-1), but with a better safety profile.

Exhibit 11: The trial design of the Phase II study in melanoma with SCIB1 in combination with pembrolizumab
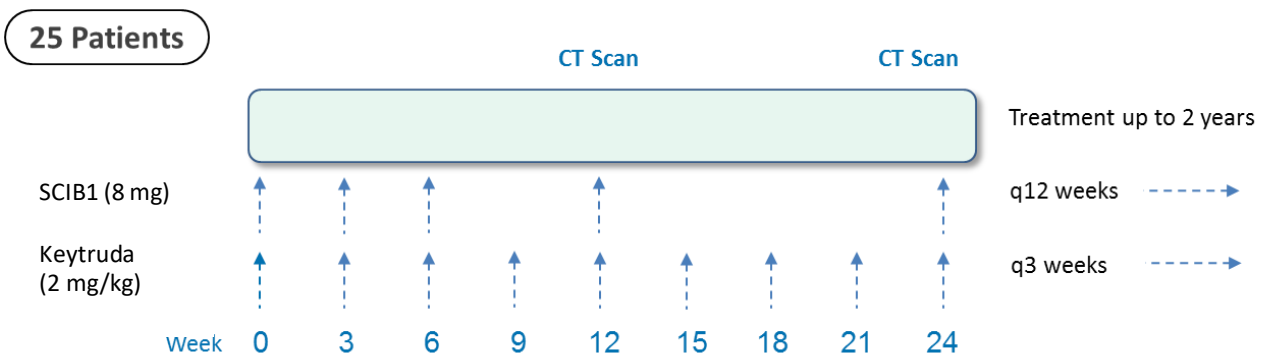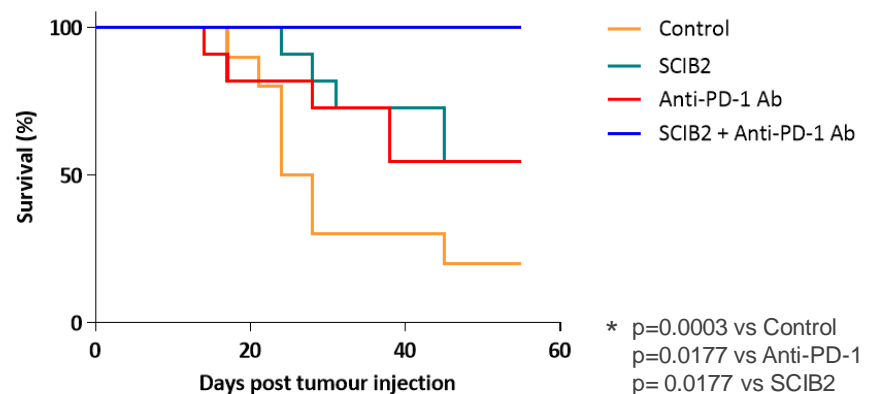

Source: Scancell

The start of the trial has been delayed slightly by FDA requesting more information, in particular about Ichor's new TriGrid 2.0 electroporation system that is due to be used in the trial (TriGrid 1.0 was used in the Phase I/II trial). The delay is not surprising as this is the first trial of SCIB1 in cancer patients in the US

and it is using the new TriGrid 2.0 system (although other companies, including Johnson & Johnson, are using it in Europe). Scancell and Ichor believe that they should be able to address all of the issues in the coming months, so that the trial can still start in H119.

Phase I/II trial with second ImmunoBody being run in collaboration with CRUK

The first clinical trial with Scancell's second ImmunoBody, SCIB2, is currently being planned with CRUK (Cancer Research UK). The Phase I/II trial will be in non-small cell lung cancer (NSCLC), and unlike with SCIB1, SCIB2 will start clinical development in combination with a checkpoint inhibitor. There is also strong preclinical data supporting the combination study approach (Exhibit 12). This Phase I/II trial will be UK-based and is being funded by CRUK.

Exhibit 12: The activity of SCIB2 and anti-PD-1 checkpoint inhibitor in combination in preclinical studies

* p=0.0003 vs Control
p=0.0177 vs Anti-PD-1
p= 0.0177 vs SCIB2

Source: Scancell

...and has broader clinical applicability

The commercial potential of SCIB2 is considerably greater than that of SCIB1, which only has potential in melanoma and a few other cancers where gp100 and TRP-2 are expressed such as glioblastoma. In contrast, SCIB2 should induce responses against the antigen NY-ESO-1, which is expressed in many different tumours (including sarcomas, neuroblastomas, myeloma, NSCLC, prostate and breast cancers). This suggests that it has the potential to be a therapeutic vaccine for most solid tumours and some haematological ones too.

Given the potential of NY-ESO-1 as a target for immunotherapies, there is much scientific interest in the antigen, but there are a limited number of therapies in development due to the challenges of targeting it (Exhibit 13 overleaf).

Competitors have struggled to show efficacy

Until recently, Immune Design was developing the therapeutic vaccine CMB305 to treat patients with NY-ESO-1 expressing tumours, but that programme has been deprioritised following analysis of Phase II data. The vaccine, which uses the company's Zvex lentivirus-based delivery system, was in a Phase III trial as monotherapy in synovial sarcoma. However, early analysis of data from a Phase II study in various sarcomas with CMB305, in combination with atezolizumab (Roche's anti PD-L1, Tecentriq), indicated that there was unlikely to be a survival benefit associated with treatment.

Exhibit 13: Therapies in clinical development targeting NY-ESO-1-expressing tumours

Product/Company	Class of therapy	Stage of development	Indications	Notes
NY-ESO SPEAR T-cells (GSK 3377794) **GlaxoSmithKline (Adaptimmune)**	T-cell therapy	Phase II	Synovial sarcoma, liposarcoma, NSCLC, melanoma, ovarian cancer and multiple myeloma	Trials as monotherapy and in combination with pembrolizumab
IMCnyeso **GlaxoSmithKline/ Immunocore**	ImmTac	Phase I/II	Melanoma, NSCLC, urothelial carcinoma, synovial sarcoma	An ImmTac is a TCR fused to an anti-CD3 domain to target and activate CD8 T cells. Patients must have have the appropriate HLA type
TAPA-pulsed DC vaccine **Kiromic**	DC vaccine	Phase I/II	Solid tumours	TAPA are tumour associated peptide antigens, which are tailored to a patient's tumours
TBI-1301 **Takara Bio**	T-cell therapy	Phase I/II	Synovial sarcoma	Partnered with Otsuka in Japan

Source: Trinity Delta

It should be noted that there were promising deep and durable responses observed in earlier trials with CMB305, validating the therapeutic vaccine approach. Unfortunately, as has been seen with other therapeutic vaccines, it appears that too few patients were able to generate sufficiently strong immune responses against the tumours following vaccination. This might be because the Zvex technology is designed to efficiently deliver the vaccine to dendritic cells; however, it does not induce cross-presentation, unlike with ImmunoBodies, which are associated with broad high-avidity responses.

Also in Q118, Celldex was developing CDX-1401 (a NY-ESO-1-antibody fusion protein, designed to direct the antigen to dendritic cells) in a Phase I/II trial in a range of solid and haematological tumours; however the programme is now on hold due to Celldex's financial issues.

Phase I/II study to be initiated by CRUK

CRUK entered into a clinical partnership agreement with Scancell and have taken on responsibility for conducting a Phase I/II trial with SCIB2 in NSCLC, in combination with a PD-1 checkpoint inhibitor. The study's primary endpoint will be safety and tolerability, but it will be interesting to see the strength of immune response and the level of tumour response following treatment, while considering the PD-L1 expression of the tumours. ImmunoBodies induce PD-L1 expression due to the release of IFNγ at the tumour site by high avidity T-cells. The overall response rate in patients with tumours that express PD-L1 strongly (tumour proportion score [TPS] ≥50%) is c30%, compared to c8% with PD-L1-negative tumours (TPS ≤1%).

Moditope platform and programme

Moditope offers a very different approach to prior technologies

The Moditope approach is quite different to other therapeutic vaccines in development, and Scancell discovered the technique with a degree of serendipity. There are many differences between the immune responses generated by Moditope and other therapeutic vaccines, but the most pertinent are the induction of CD4 cytotoxic T-cells and the strength of the response in preclinical studies to date (Exhibit 14).

Exhibit 14: Anti-tumour activity of the Moditope, Modi-1, in preclinical studies with a melanoma cancer model
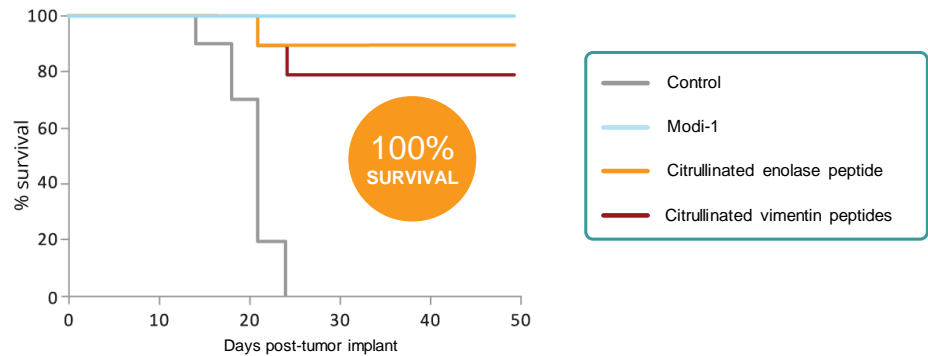
Source: Scancell; Note: Modi-1 is a therapeutic vaccine that combines citrullinated enolase peptide and citrullinated vimentin peptides, bound to TLR1/2 agonists to act as adjuvants.

A strong and sustained immune anti-tumour response

The mode of action of Moditope vaccines is illustrated in Exhibit 15. Although Moditope is a form of therapeutic vaccine, there are many differences between them and other therapeutic vaccines (including ImmunoBody), as detailed in Exhibit 16. A key point of the Moditope approach is that it effectively generates an immune response against the process of autophagy[1], which protects cells experiencing stress.

Exhibit 15: An illustration of the anti-tumour activity of Moditope
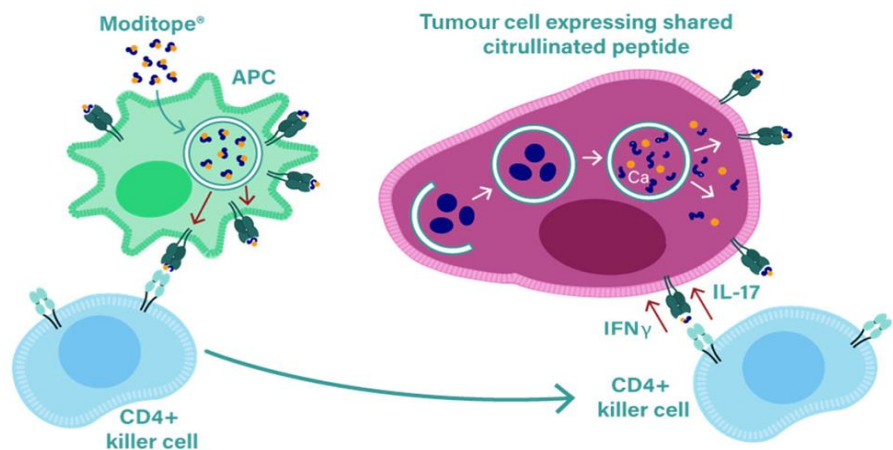
Source: Scancell; Note: This exhibit uses the example of Moditope that lead to an immune response against cells with citrullinated peptides, but they can also be used to target cells expressing peptides with other modifications.

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[1] Autophagy is the normal process that a cell uses to degrade and recycle components of a cell that are damaged or no longer required.

Exhibit 16: A comparison of characteristics of Moditope and standard therapeutic vaccines

Reason for limited efficacy	Moditope	Standard therapeutic vaccines
Antigens targeted	Common proteins (eg cytoskeletal proteins) that have post-translational modifications	Tumour-associated antigens or neo-antigens
T-cell response	Cytotoxic CD4 T-cell and CD4 Th cell	Cytotoxic CD8 T-cell and CD4 Th cell
Synergistic with checkpoint inhibitors	Potentially via indirect mechanism	Yes
Delivery system	Intra-dermal injection	Intra-dermal, intra-muscular or sub-cutaneous injection

Source: Trinity Delta

The nature of tumours means that most cancer cells live in stressful conditions that are often hypoxic and nutrient deficient. To survive in this environment, autophagy is required to recycle unwanted proteins, and dispose of damaged ones that could become toxic. During this process, the proteins that need to be removed from the cell are labelled using post-translational modifications[2], such as citrullination and homocitrullination, which results in those proteins being broken down. During this process, peptides from the modified proteins are presented on MHC II complexes which can be detected by CD4 T-cells.

Moditope may be effective in many solid tumour types

Immunisation with a Moditope generates a cytotoxic CD4 T-cell response against peptides with the post-translational modifications associated with autophagy; i.e. T-cells are produced that destroy cells that have the specific modified peptides presented by MHC II complexes. As autophagy occurs in most tumour cells, Moditope therapy has the potential to generate a potent immune response against many tumours.

Scancell has also demonstrated that Moditope generates a strong immune memory against the specific modified peptides, as shown by the preclinical studies with a tumour re-challenge assay. Consequently, Moditope vaccines could be used in the adjuvant cancer setting, to reduce the risk that a cancer patient, who has responded well to treatment, relapses.

**Tumour cells may struggle to evade Moditope's actions**

The potency of the anti-tumour response in preclinical studies suggests that tumours have limited defences against an attack from cytotoxic CD4 T-cells, unlike one from cytotoxic CD8 T-cells.

Depending on the results of the preliminary clinical trials with Moditope, it might be worth investigating the use of Moditope in combination with a checkpoint inhibitor. Indeed, the action of Moditope-induced CD4 T-cells could potentially change the tumour microenvironment, thereby converting tumours that are currently considered "cold" into "hot" ones, and therefore become responsive to checkpoint inhibitors and a cytotoxic CD8 T-cell response.

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[2] Post-translational modifications are changes that are made to a protein once it has been produced to alter its activity. Common post-translational modifications include the addition of phosphate moieties, methylation and ubiquitination.

Exhibit 17: Preclinical data indicating the ability of Moditope to generate immune memory: an anti-tumour effect is observed in melanoma model after Moditope inoculation and after re-challenge with another tumour implant.
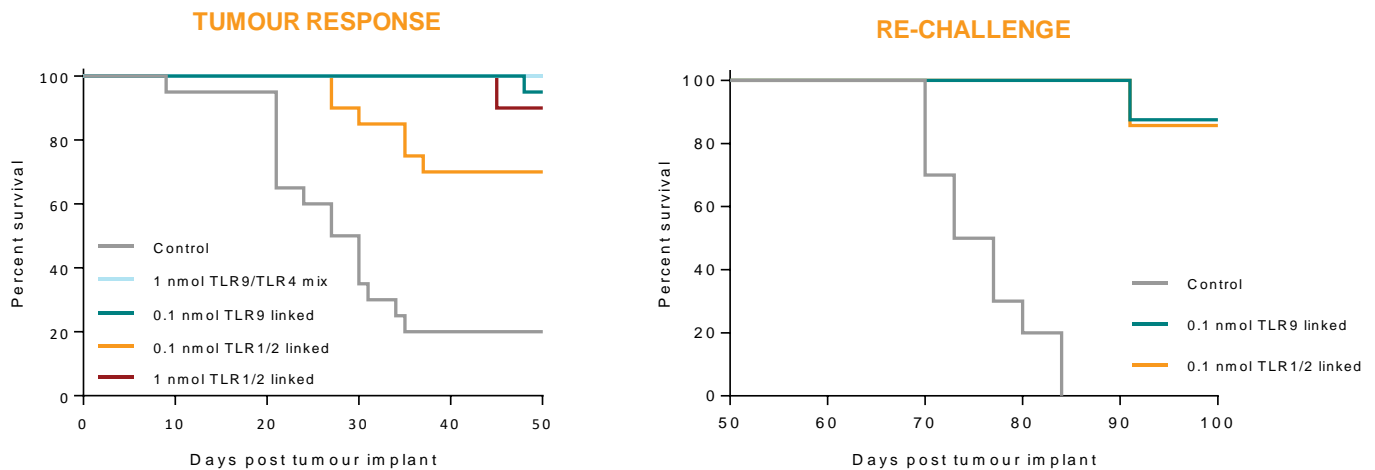
Source: Scancell

The first Moditope to enter the clinic will be Modi 1, which should begin clinical development in CY19. Modi-1 generates an immune response against citrullinated vimentin (intermediate filament protein) and enolase (glycolysis enzyme), and uses a linked TLR1/2 agonist as an adjuvant to ensure a potent T-cell response is produced. The Phase I/II trial will be a monotherapy dose-escalation trial in solid tumours such as triple negative breast cancer (TNBC), sarcoma, and ovarian cancer (Exhibit 18). The first safety and efficacy data from the study is expected during CY20.

Exhibit 18: Potential trial design of the Phase I/II study with Modi-1
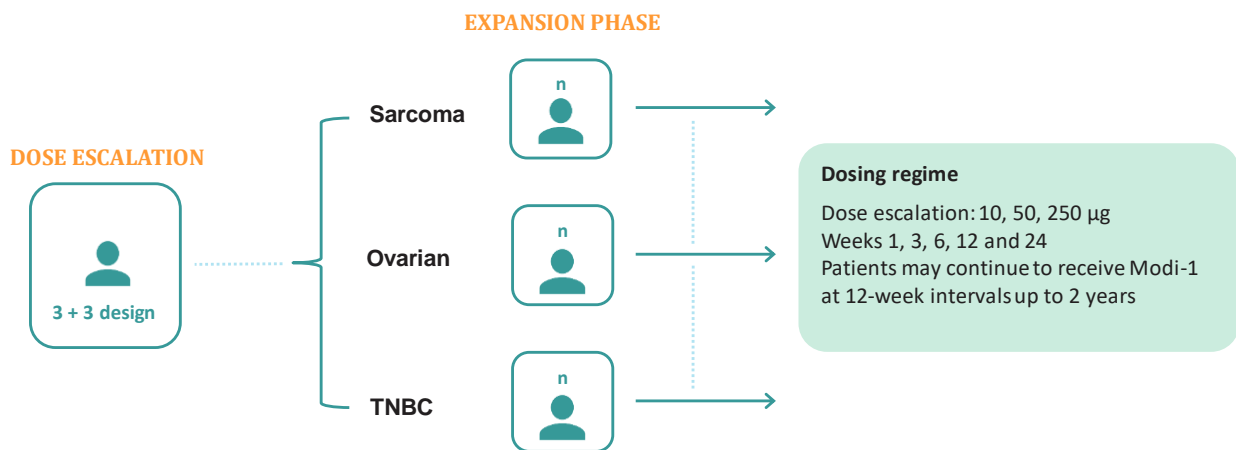
Source: Scancell

The clinical trial will exclude patients that suffer from autoimmune diseases such as rheumatoid arthritis. This is a precautionary measure as joints and tissues affected by autoimmune diseases can present citrullinated proteins to the immune system, so patients with these diseases might be more likely experience significant adverse events. Scancell has been advised by rheumatologists that this is unlikely to occur as these autoimmune diseases are caused by an inappropriate B-cell response (Th2-mediated), and not a T-cell response (Th1-mediated). Consequently, cancer patients with autoimmune diseases may be included in subsequent trials.

There are two other Moditope vaccines currently in development. Modi-2 generates a cytotoxic CD4 T-cell response against certain homocitrullinated proteins. No details of Modi-3 have been disclosed, however this programme has been short-listed for CRUK's Grand Challenge Prize for grants worth up to £20m to advance the treatment of cancer. It is a mark of Scancell's leadership in the field of immuno-oncology that it has led a team of 16 academics and companies (including Genentech and BioNTech) on to the final short-list of 10 projects from 134 applications. However, the commercial benefits of potentially being awarded the grant is less clear given uncertainty about who would own the data and the intellectual property arising from the programme.

Collaborations

The strength and quality of the underlying science at Scancell is also highlighted by its three collaborations, which are detailed below:

- **BioNTech**: The goal of the collaboration with BioNTech, formed in January 2018, is to identify and characterise T-cell receptors that recognise citrullinated vimentin and enolase (peptides that form the basis of Modi-1). At the end of the programme, BioNTech will have an exclusive option to enter into a licensing agreement to develop therapies based on the identified T-cell receptors.

- **CRUK**: The cancer charity agreed in December 2017 to fund the Phase I/II trial with SCIB2 in combination with a checkpoint inhibitor in NSCLC. At the end of the study, Scancell will have the option (no terms disclosed) to acquire the data to support the further development of SCIB2; if Scancell decides not to do so, CRUK will retain the right to advance the SCIB2 programme.

- **Karolinska Institutet**: Scancell formed the strategic collaboration with Professors Lars Klareskog and Vivianne Malmstrom in March 2016 to further explore the scientific and clinical role of citrullinated proteins in the treatment of cancer. The two Professors had previously identified the key role of citrullinated proteins in rheumatoid arthritis. This collaboration was extended in August 2018.

The BioNTech collaboration could be particularly lucrative for Scancell, with the potential of significant milestone and royalty revenues. BioNTech is the largest privately held biotech company in Europe. It aims to develop the next generation of personalised immunotherapies for cancer and other diseases, and has a $310m deal with Roche to test its personalised vaccines with Roche's atezolizumab (Tecentriq). Given the strength of preclinical responses to Scancell's Moditope, the T-cell receptors identified from the collaboration could form the basis of a class of personalised vaccine that BioNTech is looking to bring to market.

The CRUK alliance is also particularly important to the company, as it provides non-dilutive financing to advance the second ImmunoBody into the clinic and assess its potential in combination with a checkpoint inhibitor. A successful outcome to the trial would validate the potential of SCIB2 to treat the large number of tumours that express NY-ESO-1 and also of the whole ImmunoBody platform, thereby increasing significantly the value of Scancell.

Sensitivities

Risks are higher than industry average, but upside is greater too

Scancell operates at the cutting edge of the immuno-oncology segment. The attractiveness of harnessing the body's immune system to treat various tumours has attracted industry-wide attention, with numerous well-funded players operating in what has a become a crowded and competitive space. Whilst Scancell's technologies have demonstrable, and attractive, qualities it should be noted that an unexpected breakthrough in an unrelated scientific area may side-line these approaches. Clearly, even a modest success would be transformative, but the risks inherent in such research are higher than the industry average.

A wide array of immuno-oncology approaches are being explored

On the competitive front, Scancell's approach with both ImmunoBody and Moditope would be complementary to many of the methods being investigated to enhance the activity of checkpoint inhibitors, such as modulators of tryptophan catabolism and adenosine receptor activity. However, it is also competing directly against other therapeutic vaccine companies, including its collaborator BioNTech, and the various companies developing oncolytic viruses. This is an area of particular interest to big pharma companies currently (BMS has a major collaboration with PsiOxus, and Merck & Co bought Viralytics in February 2018).

Industry risks are ever-present, but manageable if understood

More generally, and in common with most innovative healthcare companies, the three main sensitivities relate to the clinical and regulatory aspects, the execution of the commercialisation plans (primarily partnership agreements), and the financial resources required to accomplish these:

- Clinical aspects– the historic failures of previous therapeutic vaccines cloud expectations of Scancell's programmes. Yet both ImmunoBody and Moditope have different mechanisms of action to any prior attempts and so should be judged on their own merits. The design and execution of the clinical programmes is an important determinant of any study outcome, but this is particularly the case in immuno-oncology trials (especially when evaluating differing therapies in combination).

- Partnership/Licensing and Exit strategies – The immuno-oncology field is particularly exciting currently, with many technologies attracting a great deal of scientific, and investor, attention. Against such a crowded and "noisy" background, it may prove difficult for Scancell to stand out sufficiently to attract the appropriate level of interest from potential partners. In fairness, the existing BioNTech collaboration suggests that good science will be appreciated, and successful innovation rewarded.

- Financial – a common refrain is that European biotech companies are seldom financed appropriately to pursue their clinical ambitions in a timely manner. This is arguably true of Scancell, where historically it has lacked the resources to progress its programmes as rapidly as was envisaged. This may yet prove to be a sensitivity in the future.

Small shareholders are sometimes "the tail wagging the dog"

Scancell has a diverse shareholder register with a large number of smaller investors; whilst many of these are well-informed and technically competent, there are a number who appear to be less aware of the risks, frustrations, and set-backs that are part and parcel of innovative drug discovery. Unfortunately, this can result in unusual share movements, especially on days with low liquidity.

Valuation

Our rNPV model suggests a value of £82.0m, or 21.1p per share

We consider an rNPV model to be the most appropriate way to value Scancell. The rNPV of each of the three individual oncology projects (adjusted for the likely success probabilities) is summed and netted against the costs of running the operation. The success probabilities are based on standard industry criteria for the respective stage of the clinical development process, but are flexed to reflect the inherent risks of the individual programme, the indication targeted, and the trial design.

As always, we employ conservative assumptions regarding market sizes and growth rates, net pricing, adoption curves, and peak market penetration. Importantly, we have valued only the clinical programmes (including those ready to enter the clinic) with nothing currently attributed to the technology platforms themselves and their use in other clinical applications. Despite such caution, this results in a valuation of £82.0m, or 21.1p per share, for Scancell (see Exhibit 19).

Exhibit 19: rNPV-based valuation of Scancell

	Total NPV (£m)	Likelihood of success	rNPV (£m)	rNPV/ share (p)	Notes
SCIB1 in melanoma	106.2	20%	18.5	4.8	Peak sales: $325m (£250m) Royalties: 17.5% Launch year: 2024
SCIB2 in NSCLC	218.7	15%	32.8	8.5	Peak sales: $843m (£648m) Royalties: 15% (net of royalties to CRUK) Launch year: 2025
Modi-1 in ovarian cancer, TNBC and sarcoma	333.1	10%	28.0	7.2	Peak sales: $1,126m (£867m) Royalties: 17.5% Launch year: 2025
G&A costs	(5.2)		(5.2)	(1.3)	
Net cash	7.9		7.9	2.0	At H119E
Total	**660.7**		**82.0**	**21.1**	
Discount rate				12.5%	
Exchange rate ($/£)				1.30	
Tax rate				10%	From 2026 with the benefit of UK Patent Box

Source: Trinity Delta

It is worth highlighting that this is a current valuation, based on the situation as we see it now, and not a price target for some time in the future. Often such price targets are expectations of what the share price should be, typically, in 12 months' time as various value inflection points are achieved.

Such price targets run counter to our conservative approach; we strive to ensure our risk-adjusted models capture the various possible scenarios, relative to both upside and downside, and then we will update our valuations as the key points are reached. Although resulting in less dramatic upside potential, we believe our valuations are more realistic, attainable and, ultimately, credible.

Progress with development will drive share price appreciation

Looking at the ImmunoBody programmes, SCIB1 is most advanced with the Phase I/II study in metastatic melanoma expected to start in H119. Assuming smooth progress, this could be commercially available by 2024 and we have modelled based on peak sales of £250m and a royalty rate of 17.5%. Using a success probability of 20%, the rNPV of this programme is £18.5m, equivalent to 4.8p a share.

Although the timings of the SCIB2 Phase I/II study in NSCLC are under the control of CRUK, we have modelled assuming a launch in 2025, peak sales of £648m, and a royalty rate of 15%. A success probability of 15% results in an rNPV of £32.8m, equivalent to 8.5p a share. The ImmunoBody platform has an rNPV of £51.4m, or 13.3p a share.

The Moditope platform is less advanced and we only consider Modi-1 in our model. This could also be commercially available by 2025, which with peak sales of £867m (across all indications currently to be studied), a royalty rate of 17.5%, and success probability of 10%, results in an rNPV of £28.0m, equivalent to 7.2p a share.

Financials

Solid control over spend has been a key feature

Over the last 18 months Scancell has made material progress on strengthening its financial position. A share placing in April 2018 at 12p per share, raised £6.9m (net), with a corresponding open offer raising a further £1.1m (net) in May 2018. At the FY18 year-end (30th April) Scancell's cash position was £10.3m. In FY18 the operating loss was £4.9m (vs £4.5m in FY17), with an overall loss of £4.2m (vs £3.5m). The largest expenditures were development costs of £2.9m (up 3% on FY17 of £2.8m) and administrative expenses of £2.1m (up 17% on FY17 of £1.8m). The increase in administrative costs was driven by an increase in licensing and patent costs for the ImmunoBody and Moditope platforms.

Clinical programmes means cash burn is expected to rise

Looking ahead, for FY19 we expect the operating loss to widen to £8.6m, with the overall loss rising to £7.1m. This is driven by development costs forecast to grow to £6.1m, as clinical programmes start their ramp up. General and administrative expenses are expected to increase to £2.5m. For FY20 we expect these expenses to be just over £5.0m and £2.6m respectively, with an operating loss of £7.6m and overall loss of £6.4m. The reduction in R&D costs in FY20 is because of the costs of producing drug substances and other upfront costs associated with the clinical trials in the previous year. The resulting cash outflows mean we are expecting the cash position to be £4.3m at end-FY19 and so are forecasting a funding requirement of c £12m by FY20 (assuming spending on clinical programmes is maintained as planned).

A stronger balance sheet would help maintain focus and progress

This funding requirement may be satisfied, in part at least, through non-dilutive funding (such as grants and awards) or partnership/licensing agreements. However, we believe that Scancell has suffered historically through having insufficient capital to progress its programmes as rapidly as it should have. In order to not be similarly hampered at such a time-sensitive stage, we would advocate that an equity raise sufficient to ensure financial stability would be advisable. Certainly, management appreciates the size of the commercial opportunity, and has grasped the importance of sensible investment in the clinical programmes and of ensuring the appropriate infrastructure is in place to support them in the very competitive immuno-oncology market. Whilst sensible cost control should remain in place, judicious investment to progress the programmes should be encouraged.

Exhibit 20: Summary of financials

Year-end: April 30	£'000s	2016	2017	2018	2019E	2020E	2021E
INCOME STATEMENT							
Revenues		**0**	**0**	**0**	**0**	**0**	**0**
Cost of goods sold		0	0	0	0	0	0
Gross Profit		**0**	**0**	**0**	**0**	**0**	**0**
R&D expenses		(2,009)	(2,766)	(2,855)	(6,107)	(5,037)	(6,044)
General and administrative expenses		(1,034)	(1,783)	(2,087)	(2,537)	(2,598)	(2,678)
Underlying operating profit		**(3,043)**	**(4,549)**	**(4,942)**	**(8,645)**	**(7,635)**	**(8,722)**
Other revenue/expenses		0	0	0	0	0	0
EBITDA		**(3,021)**	**(4,516)**	**(4,914)**	**(8,617)**	**(7,612)**	**(8,698)**
Operating Profit		**(3,043)**	**(4,549)**	**(4,942)**	**(8,645)**	**(7,635)**	**(8,722)**
Interest expense		14	53	3	18	6	20
Profit Before Taxes		**(3,030)**	**(4,495)**	**(4,939)**	**(8,626)**	**(7,629)**	**(8,702)**
Adj. PBT		**(3,030)**	**(4,495)**	**(4,939)**	**(8,626)**	**(7,629)**	**(8,702)**
Current tax income		446	950	745	1,527	1,259	1,511
Cumulative preferred stock dividend		0	0	0	0	0	0
Net Income		**(2,583)**	**(3,545)**	**(4,195)**	**(7,099)**	**(6,370)**	**(7,191)**
EPS (p)		**(1.1)**	**(1.4)**	**(1.3)**	**(1.8)**	**(1.6)**	**(1.9)**
Adj. EPS (p)		**(1.1)**	**(1.4)**	**(1.3)**	**(1.8)**	**(1.6)**	**(1.9)**
DPS (p)		**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Average no. of shares (m)		227.6	261.6	312.7	387.8	387.8	387.8
Gross margin		*N/A*	*N/A*	*N/A*	*N/A*	*N/A*	*N/A*
BALANCE SHEET							
Current assets		**7,088**	**3,523**	**11,145**	**5,359**	**11,019**	**3,859**
Cash and cash equivalents		6,527	2,672	10,303	4,328	10,026	2,803
Accounts receivable		121	102	97	97	97	97
Inventories		0	0	0	0	0	0
Other current assets		440	749	745	934	896	959
Non-current assets		**3,480**	**3,508**	**3,492**	**3,479**	**3,475**	**3,473**
Property, plant & equipment		65	93	77	64	60	57
Other non-current assets		0	0	0	0	0	0
Current liabilities		**(576)**	**(532)**	**(696)**	**(696)**	**(12,696)**	**(12,696)**
Short-term debt		0	0	0	0	(12,000)	(12,000)
Accounts payable		(576)	(532)	(696)	(696)	(696)	(696)
Other current liabilities		0	0	0	0	0	0
Non-current liabilities		**0**	**0**	**0**	**0**	**0**	**0**
Long-term debt		0	0	0	0	0	0
Other non-current liabilities		0	0	0	0	0	0
Equity		**9,992**	**6,499**	**13,941**	**8,142**	**1,798**	**(5,364)**
Share capital		22,047	22,047	33,749	35,026	35,026	35,026
Other		(12,055)	(15,548)	(19,808)	(26,884)	(33,228)	(40,391)
CASH FLOW STATEMENTS							
Operating cash flow		**(2,327)**	**(3,841)**	**(4,060)**	**(7,238)**	**(6,283)**	**(7,201)**
Profit before tax		(3,030)	(4,495)	(4,939)	(8,626)	(7,629)	(8,702)
Non-cash adjustments		44	31	(41)	33	43	32
Change in working capital		(12)	(25)	169	0	0	0
Interest paid		4	6	3	18	6	20
Taxes paid		667	642	749	1,337	1,297	1,448
Investing cash flow		**10**	**(14)**	**(11)**	**(15)**	**(19)**	**(21)**
CAPEX on tangible assets		0	(61)	(11)	(15)	(19)	(21)
Other investing cash flows		10	47	0	0	0	0
Financing cash flow		**5,786**	**0**	**11,702**	**1,277**	**12,000**	**0**
Proceeds from equity		5,786	0	11,702	1,277	0	0
Increase in loans		0	0	0	0	12,000	0
Other financing cash flow		0	0	0	0	0	0
Net increase in cash		**3,468**	**(3,855)**	**7,631**	**(5,976)**	**5,698**	**(7,223)**
Cash at start of year		3,059	6,527	2,672	10,303	4,328	10,026
Cash at end of year		**6,527**	**2,672**	**10,303**	**4,328**	**10,026**	**2,803**
Net cash at end of year		**6,527**	**2,672**	**10,303**	**4,328**	**(1,974)**	**(9,197)**

Source: Scancell, Trinity Delta Note: Adjusted numbers exclude exceptionals.

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Key personnel

Person	Position	Biography
Dr John Chiplin	Non-Executive Chairman	Joined as Chairman in May 2016. Founder and Managing Director of Newstar Ventures Ltd. Previously CEO of Polynoma, Arana Therapeutics, Geneformatics, and ITI (Intermediary Technology Institute). Non-executive director of numerous companies, both public and private. Holds a BPharm (Hons) and PhD from the University of Nottingham
Dr Cliff Holloway	CEO	Joined as CEO in January 2018. Over 25 years experience of CEO, COO, Business Development roles with Benitec Biopharma, Sienna Cancer Diagnostics, Immune Systems Therapeutics, Biosceptre International, Arana Therapeutics, and Teva Pharmaceuticals Australia. Holds a BPharm (Hons) and a PhD in Medicinal Chemistry from the University of Nottingham.
Professor Lindy Durrant	CSO	Founded Scancell in January 1996 as a spin-out from work she performed at the University of Nottingham (which she joined in December 1983). An internationally recognised tumour immunologist, she is currently Professor of Cancer Immunology at the Department of Clinical Oncology. Over 120 publications in peer-reviewed journals and over 10 patents filed. Gained a BSc (Hons) in Biochemistry and a PhD from Manchester University.
Dr Sally Adams	Development Director	Appointed as Development Director in May 2014 having previously worked as a development consultant to Scancell, providing guidance on the development of SCIB1, She was Head of Neurology & Virology at British Biotech and Development Director at Neures Limited before becoming an independent consultant providing drug development and management services within the biotechnology and pharmaceutical sectors, specialising in biological entities.

Keith Green	Director of Finance	Joined on a part-time basis in January 2010 and became full-time in September 2016. Fifteen years experience with private and AIM listed companies in the Life Sciences sector. Previously twenty years experience as an accountant. Trained and qualified as a Chartered Accountant with Peat Marwick (now part of KPMG).

Top institutional shareholdings

	% holding
Calculus Capital	12.9
City Financial Investment Company	5.6
Directors and related holdings	5.0
Legal & General Investment Management	4.7
Hygea VCT	3.4
Top institutional investors	31.6
Other shareholders	68.4
Total shareholders	100.0

Source: Scancell

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More information is available on our website: www.trinitydelta.org